MARKED-UP COPY OF THE AMENDMENTS

Claims 2-11 and 15-19 have been canceled.

New claims 20-26 have been added as follows (comparison with corresponding canceled claims show deleted portions stricken out and added portions in bold):

20. (New, corresponds to amended claim 18) A fusion protein comprising (i) ~~a polypeptide~~ **an antigenic protein derived from** Mycoplasma gallisepticum causing an antibody-antigen reaction with Mycoplasma gallisepticum immune serum or Mycoplasma gallisepticum infected serum ~~and having an epitope of Mg polypeptide showing antigenicity;~~ and (ii) a **signal** polypeptide ~~having at least one epitope~~ of Herpesvirus outer membrane protein, said **signal** polypeptide ~~having at least one epitope of Herpesvirus outer membrane protein~~ being ligated with ~~the polypeptide causing an antibody-antigen reaction with Mycoplasma gallisepticum immune serum or Mycoplasma gallisepticum infected serum and having an epitope of native Mg polypeptide showing antigenicity~~ **said antigenic protein derived from** Mycoplasma gallisepticum at the N terminus thereof.

21. (New) A fusion protein according to claim 20, wherein a sequence of said antigenic protein is amino acids 64-456 of SEQ ID NO:2 or amino acids 693-1086 of SEQ ID NO:4.

22. (New, corresponds to three times amended claim 2) A fusion protein according to claim ~~18~~ **20**, wherein said ~~outer membrane protein~~ **signal polypeptide** is derived from a herpes virus showing infection to fowl.

23. (New, corresponds to three times amended claim 3) A fusion protein according to claim ~~2~~ **22**, wherein said ~~outer membrane protein~~ **signal polypeptide** is derived from a Marek's disease virus.

24. (New, corresponds to three times amended claim 4) A fusion protein according to claim ~~3~~ **23**, wherein said ~~outer membrane protein~~ **signal polypeptide** is gB protein derived from a Marek's disease virus.

25. (New, corresponds to three times amended claim 11) A recombinant Avipox virus in which a DNA coding for the fusion protein according to ~~any one of claims 1 to 8~~ **claim 20** has been inserted.

26. (New, corresponds to twice amended claim 16) A recombinant live vaccine for anti-fowl Mycoplasma gallisepticum infection comprising as an effective ingredient a recombinant Avipox virus in which a DNA coding for the fusion protein according to ~~any one of claims 2 through 8 and 18~~ **claim 20** has been inserted, wherein the fusion protein is capable, upon administration into a host cell, of immunizing that cell against subsequent infection with Mycoplasma gallisepticum.

REMARKS

By the present amendment, claims 2-11 and 15-19 have been canceled and new claims 20-26 have been added.

Claims 20-26 are pending in the present application. Claims 20-24 are directed to a fusion protein, claim 25 is directed to a recombinant Avipox virus, and claim 26 is directed to a recombinant live vaccine.

In paragraphs 3 and 6 of the Office Action, claims 2-11 and 15-19 are rejected under 35 U.S.C. 112, first paragraph, for lack of enablement and lack of written description, respectively. Is alleged in the Office Action that the description of "a polypeptide causing an antibody-antigen reactions and having a epitope and a polypeptide having a epitope of Herpesvirus outer membrane protein" is insufficient in the absence of a description of the "detailed structure" with reduction to practice.

Reconsideration and withdrawal of the rejections is respectfully requested.

As a preliminary, the recitation "a polypeptide having at least one epitope of Herpesvirus outer membrane protein" in claim 18 is no longer present in claim 20 which recites "a signal polypeptide of Herpesvirus outer membrane protein."

Further, it is submitted that the signal sequence of a Herpesvirus outer membrane protein is taught in the present specification. Specifically, on page 8, lines 16-17 of the specification, a variety of glycoproteins are mentioned as the outer membrane protein of the herpes virus. It is also indicated that the signal sequence is detectable at the carboxyl terminus or amino terminus of the outer membrane protein, and that the signal sequence is detectable in the hydrophobic peptide region. In addition, a particular signal sequence of gB protein derived from a Marek's

disease virus (MDV) is disclosed, in particular on page 10, lines 13-25, from which it is clearly understood that the exemplary signal sequence is found in amino acids 1-63 of SEQ ID NO:2.

On the basis of these general and specific teachings in the specification, a person of ordinary skill in the art would have sufficient guidance to determine an appropriate signal sequence of Herpesvirus outer membrane protein. Such determination would rely in particular, on the teaching in the present specification that the hydrophobicity of the signal region is of great importance. It is well known that amino acids showing hydrophobicity include phenylalanine, tryptophan, isoleucine, leucine, proline, methionine, valine and alanine. Accordingly, determination of appropriate signal regions would not require undue experimentation based on the specification teachings and the knowledge of a person of the art.

Also, with respect to the antigenic protein, the epitope of the antigenic protein region varies for every antigenic protein, but the method for determining the epitope region is disclosed in the present specification, in particular from page 6, line 23 to page 7, line 4, and is exemplified for Mycoplasma gallisepticum in the passage starting at page 7, line 5.

In view of the above, it is submitted that the specification is sufficiently descriptive and enabling with respect to the present claims. Therefore, it is submitted that the rejections should be withdrawn.

Next, in paragraph 4 of the Office Action, claims 16-17 are rejected under 35 U.S.C. 112, first paragaph, for lack of enablement. It is alleged that the specification does not enable "vaccines" in the absence of protocols, formulations, and immunological experiments showing effectivity against Mg, and in the absence of identification of "the epitopes and the make up of the polypeptides involved."

Reconsideration and withdrawal of the rejection is respectfully requested. As a preliminary, claims 16-17 have been canceled and present claim 26 is directed to a vaccine.

Further, it is submitted that Examples 5-6 of the present specification report comparative experiments on the antibody-inducing capability and resistance to challenge with Mg, respectively, using a vaccine as recited in present claim 26. Thus, a person of ordinary skill in the art would find guidance and an expectation of success in preparing and testing a vaccine according to the claimed invention, so that no undue experimentation would be required. Therefore, the specification is enabling for present claim 26.

In view of the above, it is submitted that the rejection should be withdrawn.

Next, in paragraph 5 of the Office Action, claim 19 is rejected under 35 U.S.C. 112, first paragraph, for lack of enablement. It is alleged that amino acid substitution is not predictable and no guidance is provided as to amino acid selection to obtain 90% homology.

As claim 19 has been canceled, this rejection is moot.

Next, in paragraphs 7 and 11-13 of the Office Action, claims 2-12 and 15-17 are rejected under 35 U.S.C. 112, second paragraph, as indefinite. In paragraph 7 of the Office Action, it is alleged that the term "capable of immunizing" in claim 17 is unclear. In paragraph 11 of the Office Action, it is alleged that the term "derived" in claims 5, 7-8, and 15 is too vague. In paragraph 12 of the Office Action, it is alleged that the recitation of DNA coding for the fusion protein in claims 9-12 is indefinite and unclear in the absence of specific DNA sequence. In paragraph 13 of the Office Action, it is alleged that the recitation of the polypeptides in claims 16-17 is not defined as to "specific protein size, sequence or amino acid fragment."

Reconsideration and withdrawal of the rejections is respectfully requested. As to the rejection set forth in paragraph 7, claim 17 has been canceled, so that this rejection is moot. As to the rejection set forth in paragraph 11, it is submitted that the term "derived" in claims 23-25 is sufficiently clarified by the recitation present in claim 20 of "a signal polypeptide of Herpesvirus outer membrane protein." As to the rejection set forth in paragraph 12, it is submitted that a person of ordinary skill in the art would find sufficient guidance in the specification to determine the corresponding DNA sequences, as discussed above with respect to the rejections set forth in paragraphs 3 and 6. As to the rejection set forth in paragraph 13, it is submitted that the polypeptide of present claim 26 is sufficiently disclosed in view of the recitation of present claim 20, as well as the corresponding explanations and exemplifications in the specification.

In view of the above, it is submitted that the indefiniteness rejections should be withdrawn.

Next, in paragraph 8 of the Office Action, claims 2-11 and 15-19 are objected to for informalities because of the recitation "Mg" in claim 18 and an allegedly improper dependency of claim 16.

The present claims do not recite "Mg" and present claim 26 depends on claim 20 only. Accordingly, it is submitted that the objections should be withdrawn.

Next, in the Office Action, claims 2-10, 15 and 17-19 are rejected under 35 U.S.C. 103(a) as obvious over WO 94/23019 which names Sajto as an inventor ("**Sajto**") in view of Yoshida et al., Virology, Vol. 200 (1994) ("**Yoshida**"); and claims 11 and 16 are rejected under 35 U.S.C. 103(a) as obvious over **Sajto** in view of **Yoshida**, and further in view of ("**Yangida**") (paragraphs 9, 14-15 of the Office Action). In summary, it is alleged that **Sajto** discloses the subject matter

of claims 1-10, 15 and 17-19 except the polypeptide derived from a Herpes outer membrane protein, and that **Yoshida** "suggests that FPV is a good candidate for an MDV vaccine and that gB is an important target for the host immune response," so that it would have been obvious to use the polypeptide derived from **Yoshida** with the fusion protein of **Sajto**. Further, with respect to claims 11-12, it is alleged that **Yangida** "teaches that recombinant Avipoxvirus genes are effective as vaccine," so that it would have been obvious to use the recombinant Avipox virus of **Yangida** with the fusion polypeptide of **Yoshida** and **Sajto**.

Reconsideration and withdrawal of the rejection is respectfully requested.

The present inventors have established that the following effects can be obtained by inserting in a recombinant Avipox virus and expressing fusion genes coding for an antigenic gene of Mycoplasma gallisepticum ligated to a signal sequence of Herpesvirus outer membrane protein:

- a vaccine effect is considerably improved, as compared to the expression of only the antigenic gene not ligated to DNA sequences coding for the signal;
- a vaccine effect is considerably improved, as compared to the expression of fusion genes comprising DNA sequences coding for the an antigenic gene of Mycoplasma gallisepticum ligated to a signal of New Castle disease (NDV), as disclosed in **Sajto**.

Specifically, the fusion genes comprising DNA sequences coding for the an antigenic gene of Mycoplasma gallisepticum ligated to a signal of NDV, as disclosed in **Sajto**, induces neutralizing antibodies in vitro, but does not prevent infection in vivo. None of the cited references teaches or suggests that the fusion gene of **Sajto** has any immunological effect in vivo, and none of the cited references teaches or suggests using a signal sequence of the gB gene derived from Marek's disease virus (MDV) instead of the signal of NDV used by **Sajto**.

Reference is made in particular to the Declaration under Rule 1.132 which was submitted on June 27, 2000. The experimental data reported in Example 6 of the present specification and in the Declaration show that the fusion protein of the presently claimed invention provides considerably improved effects, as compared to the fusion protein of **Sajto**. In particular, as can be seen in the Declaration, chicken inoculated with the recombinant viruses of **Sajto** (fNZ929-67, fNZ7929-66 and fNZ2929XM1) do not have an improved immunological response, as compared with non-inoculated chicken, which shows that the recombinant viruses of **Sajto** are not useful as vaccines for anti-Mycoplasma infection.

In addition, the signal sequence of the presently claimed invention, which is a hydrophobic peptide, enable extracellular secretion of the antigenic proteins of Mycoplasma gallisepticum, by contributing to the approach of the antigenic protein to the lipid bilayer of cell membranes and the passage of the membranes.

Finally, **Yoshida** discloses a recombinant virus in which the gB gene of MDV is incorporated, including a signal sequence as in the Examples of the present specification in the gB gene. However, **Yoshida** fails to teach or suggest that the signal sequence is combined with an antigenic gene other than MDV. Therefore, there would be no motivation to combine **Yoshida** with the other cited references.

In view of the above, the present claims are not obvious over any combination of the cited references. Therefore, it is submitted that the prior art rejections should be withdrawn.

In conclusion, the invention as presently claimed is patentable. It is believed that the claims are in allowable condition and a notice to that effect is earnestly requested.

In the event there is, in the Examiner's opinion, any outstanding issue and such issue may be resolved by means of a telephone interview, the Examiner is respectfully requested to contact the undersigned attorney at the telephone number listed below.

In the event this paper is not considered to be timely filed, the Applicants hereby petition for an appropriate extension of the response period. Please charge the fee for such extension and any other fees which may be required to our Deposit Account No. 01-2340.

Respectfully submitted,

ARMSTRONG, WESTERMAN, HATTORI,
McLELAND & NAUGHTON, LLP

By: Nicolas Seckel

Nicolas E. Seckel
Attorney for Applicants
Reg. No. 44,373

Atty. Docket No. 981167

Suite 1000
1725 K Street, N.W.
Washington, D.C. 20006
Tel: (202) 659-2930
Fax: (202) 887-0357

NES:rep